REMARKS

Claims 11-14 are pending in the subject application. Entry of this Amendment and reconsideration of the application are respectfully requested.

I. Obviousness Rejections under 35 U.S.C § 103(a)

Claims 11-14 stand rejected under 35 U.S.C § 103(a) as being allegedly obvious over U.S. Patent No. 6,476,043 B1 to Toutain et al. ("Toutain") or U.S. Patent No. 6,545,010 B2 to Bissery ("Bissery") for the "reasons of record."[1] In particular, the Examiner states that "it was clearly stated in the last office action that the therapeutic effect of instant composition is solely due to irinotecan and the therapeutic utility of irinotecan is well known in the prior art." The Examiner contends that "[t]he Applicants have not provided any unexpected results of either superior activity or reduced side effects by the instant combination over the prior art known composition comprising irinotecan." Applicant respectfully traverses these rejections.

1. Claims 11-14 are not Obvious over Toutain

In the Office Action mailed on September 14, 2004 ("the September 2004 Office Action"), the Examiner stated that "Toutain discloses use of camptothecin derivatives, with reduced gastrointestinal toxicity. The medicinal product of pharmaceutical compositions disclosed by Toutain (see claims 1-5) meets all the limitations except that it does not mention detectable amount of 4-amino-3-propionylphenyl-1.4'-bipiperidine-1'-carboxylate in the composition." In the September 2004 Office Action, the Examiner further stated that "Toutain teaches the utility of irinotecan for treating cancer (see claims 6-12)." The Examiner asserted that "[i]t is also well established in the prior art to combine the main therapeutic compound with other compounds in order to produce a synergistic effect or reduce it's [sic] side effects as combined by Toutain (see composition claims 1-5 as well as method claims 6-12)." In the September 2004 Office Action, the Examiner contended that "it would have been obvious to one skilled in the art to prepare the instant composition without losing its therapeutic utility for treating cancer." Applicant respectfully disagrees.

The claims of the present invention are directed to "a pharmaceutical composition comprising irinotecan and/or at least one salt thereof in a therapeutically effective amount and 4-amino-3-propionylphenyl-1,4'-bipiperidine-1'-carboxylate and/or at least one salt

[1] The basis of the rejection is set forth in an Office Action mailed on September 14, 2004 and an Office Action mailed _____.

thereof in a detectable amount." As taught by Applicant, "the presence of 4-amino-3-propionylphenyl-1,4'-bipiperidine-1'-carboxylate in a drug substance of this embodiment is useful as an analytical marker" (page 6, paragraph **[0021]**). Toutain does not teach or suggest a composition containing any analytical marker, let alone a composition comprising 4-amino-3-propionylphenyl-1,4'-bipiperidine-1'-carboxylate which functions, *e.g.*, as an analytical marker. Thus, assuming *arguendo* that 4-amino-3-propionylphenyl-1,4'-bipiperidine-1'-carboxylate does not reduce the side effects associated with irinotecan, or that the combination of 4-amino-3-propionylphenyl-1,4'-bipiperidine-1'-carboxylate and irinotecan produces no synergistic effect, one skilled in the art would still find no motivation or suggestion in Toutain to make or use a composition containing a detectable amount of 4-amino-3-propionylphenyl-1,4'-bipiperidine-1'-carboxylate either for its therapeutic effect or as an analytical marker.

"To establish prima facie obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art." MPEP § 2143.03 (citing *In re Royka*, 490 F.2d 981 (Fed. Cir. CCPA 1974)).

In summary, and as conceded by the Examiner, Toutain does **not** teach or even suggest a composition containing 4-amino-3-propionylphenyl-1,4'-bipiperidine-1'-carboxylate and any camptothecin derivative, let alone irinotecan. Moreover, Toutain does not teach or even suggest that compositions containing irinotecan should contain any analytical marker, let alone the 4-amino-3-propionylphenyl-1,4'-bipiperidine-1'-carboxylate that is recited the claims of the present invention. Because Toutain does not teach or suggest a composition containing irinotecan and 4-amino-3-propionylphenyl-1,4'-bipiperidine-1'-carboxylate in a detectable amount as recited in the claims of the present invention, the Examiner has not established prima facia obviousness as required by *In re Royka*,. Therefore, Applicant respectfully submits that claims 11-14 are not obvious over Toutain, and requests that the rejection of claims 11-14 under 35 U.S.C § 103(a) be withdrawn.

2. **Claims 11-14 are not Obvious over Bissery**

In the September 2004 Office Action the Examiner stated that "Bissery disclosed composition [sic] comprising camptothecin or camptothecin derivative and a platin derivative for the treatment of cancer." The Examiner asserted that "[t]he pharmaceutical composition disclosed by Bissery (see claim 16) meets all the limitations except that it does not contain detectable amount of 4-amino-3-propionylphenyl-1,4'-bipiperidine-1'-carboxylate in the

composition." In the September 2004 Office Action the Examiner further asserted that "Bissery teaches the utility for treating cancer (see claims 1-15). It is also well established in the prior art to combine the main therapeutic compound with other compounds in order to produce a synergistic effect or reduce it's [sic] side effect as combined by Bissery (see composition claim 16 as well as method claims 1-15)." In the September 2004 Office Action the Examiner still further asserted that "[i]n the instant composition, the therapeutic effect is solely due to irinotecan and therefore, in absence of some unexpected results of superior activity or reduced side effects by the instant combination over the prior art known composition comprising irinotecan, it would have been obvious to one skilled in the art to prepare the instant compositions without its therapeutic utility for treating cancer." Applicant respectfully disagrees.

As noted above, the claims of the present invention are directed to "a pharmaceutical composition comprising irinotecan and/or at least one salt thereof in a therapeutically effective amount and 4-amino-3-propionylphenyl-1,4'-bipiperidine-1'-carboxylate and/or at least one salt thereof in a detectable amount." As taught by Applicant, "the presence of 4-amino-3-propionylphenyl-1,4'-bipiperidine-1'-carboxylate in a drug substance of this embodiment is useful as an analytical marker" (page 6, paragraph **[0021]**). Thus, assuming *arguendo* that 4-amino-3-propionylphenyl-1,4'-bipiperidine-1'-carboxylate does not reduce the side effects associated with irinotecan, or that the combination of 4-amino-3-propionylphenyl-1,4'-bipiperidine-1'-carboxylate and irinotecan produces no superior results, one skilled in the art would still find no motivation or suggestion in Bissery to make or use a composition containing a detectable amount of 4-amino-3-propionylphenyl-1,4'-bipiperidine-1'-carboxylate either for its therapeutic effect or as an analytical marker.

In summary, and as conceded by the Examiner, Bissery does **not** teach or even suggest a composition containing 4-amino-3-propionylphenyl-1,4'-bipiperidine-1'-carboxylate and any camptothecin derivative, let alone irinotecan. Moreover, Bissery does not teach or even suggest that compositions containing irinotecan should contain any analytical marker, let alone the 4-amino-3-propionylphenyl-1,4'-bipiperidine-1'-carboxylate as taught in the present specification. Because Toutain does not teach or suggest a composition containing irinotecan and 4-amino-3-propionylphenyl-1,4'-bipiperidine-1'-carboxylate in a detectable amount as recited in the claims of the present invention, the Examiner has not established prima facia obviousness as required by *In re Royka*, 490 F.2d.

981 ("To establish prima facie obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art.").

Therefore, Applicant respectfully submits that claims 11-14 are not obvious over Bissery, and requests that the rejection of claims 11-14 under 35 U.S.C § 103(a) be withdrawn.

II. Rejection of Claims 11-14 under the Judicially Created Doctrine of Obviousness Double Patenting

The Examiner rejected claims 11-14 under the judicially created doctrine of double patenting as being unpatentable over claims 6 and 7 of U.S. Patent No. 6.723,729 to Henegar et al. ("Henegar"). The Examiner concedes that "the conflicting claims are not identical." Nevertheless, the Examiner asserts that "they are not patentably distinct from each other because irinotecan or a salt prepared by using 4-amino-3-propionylphenyl-1,4'-bipiperidine-1'-carboxylate or a salt is claimed in the cited patent and furthermore, the therapeutic utility for treating cancer is well known in the prior art."

Applicant do not agree with the Examiner's position on this rejection; however, in order to advance prosecution, Applicant will submit a terminal disclaimer in compliance with 37 CFR § 1.321(c) once the claims are found otherwise allowable.

Conclusion

In view of the above remarks, Applicant submits that the present claims are now in condition for allowance. Applicant does not believe any additional fee(s) are due in connection with this Amendment. However, if any additional fee(s) is due, Applicant's attorney authorizes payment from deposit account number 16-1445 or the credit of any overpayment to the aforementioned deposit account.

If the Examiner wishes to comment or discuss any aspect of this application or response, Applicant's undersigned attorney invites the Examiner to call him at the telephone number provided below.

Respectfully submitted,

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